



## EXCEPTIONAL CASE

# Elevation of serum creatinine in a renal transplant patient following oral creatine supplementation

Jonathan Philip Law, Saveria Di Gerlando, Tanya Pankhurst and Lavanya Kamesh

Department of Renal Medicine, University Hospitals Birmingham NHS Foundation Trust, Birmingham, UK

Correspondence and offprint requests to: Jonathan Philip Law; E-mail: [jonathan.law@uhb.nhs.uk](mailto:jonathan.law@uhb.nhs.uk); Twitter handle: @milkpowder

## ABSTRACT

We report the case of a renal transplant recipient presenting with elevated serum creatinine levels whilst taking oral creatine ethyl ester (CEE), but not creatine monohydrate (CM). Standard investigations for allograft dysfunction, including Doppler ultrasound and renal biopsy, were normal. Serum creatinine normalized following cessation of the supplement. CM is poorly absorbed and does not affect creatinine. In contrast, CEE is converted and absorbed as creatinine, elevating serum levels. In such cases, creatinine is not a valid surrogate for glomerular filtration rate (GFR). Alternate methods of GFR measurement should be considered and a rigorous clinical and drug history taken.

**Keywords:** creatinine, creatine supplements, creatine ethyl ester, GFR, nutrition

## BACKGROUND

Oral creatine supplements are widely taken to enhance muscle function and athletic performance [1]. To date, there is an absence of literature reporting serum creatinine (Cr) rise following ingestion of creatine in a renal allograft patient.

## CASE REPORT

We report the case of a 29-year-old Caucasian male presenting with elevated serum Cr levels on routine renal transplant clinic bloods whilst taking creatine ethyl ester (CEE) supplementation. The patient was 18 months post-transplant with stable 10-month median Cr of 108  $\mu\text{mol/L}$  receiving standard immunosuppression: tacrolimus, prednisolone and mycophenolate mofetil. Other medications included bisoprolol, ferrous sulphate and ranitidine. Routine clinic bloods revealed a serum Cr of 245  $\mu\text{mol/L}$  with no change in urea (11.7 mmol/L) from baseline (Figure 1). All other standard bloods were within normal range.

He had also been taking 3.2 g/day of CEE in the preceding month and prior to this, 5 g/day of creatine monohydrate (CM) for 6 months. He reported no ill effects and denied taking non-prescribed medications.

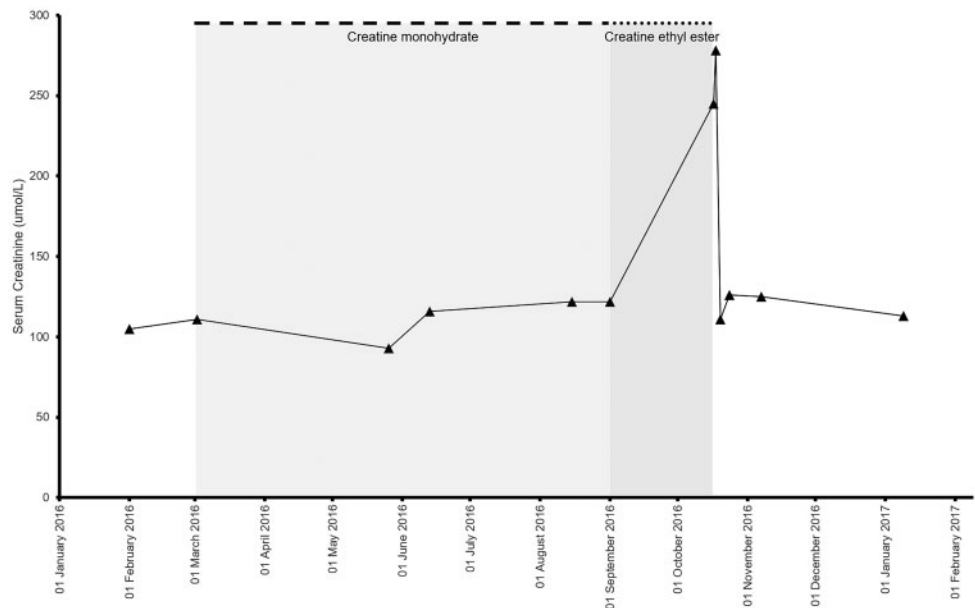
Physical examination revealed a muscular physique weighing 77.6 kg (Body Mass Index 25.9 kg/m<sup>2</sup>). Precordial, pulmonary and abdominal examinations were unremarkable and the patient was intravascularly replete. Blood pressure was 139/76 mmHg.

Further investigations were performed. Serum polyomavirus PCR was undetectable. Tacrolimus trough level was 5.8 ng/mL and donor-specific Human Leukocyte Antigen Class I/II antibodies were negative. Midstream urine was negative for infection and albumin: Cr ratio was 1.1 mg/mmol. Doppler ultrasound of the allograft demonstrated patent vessels, normal intrarenal resistive indices and no hydronephrosis. A kidney biopsy showed no evidence of acute or chronic tubular damage, nor were there signs of antibody or T cell-mediated rejection or calcineurin inhibitor toxicity. Immunostaining for SV40 and C4d was

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**FIGURE 1:** CM ingestion (shaded area under dashed line) did not alter serum Cr, which rose acutely after patient switched to taking CEE (shaded area under dotted line). Serum Cr returned to baseline after cessation of the supplement.

negative. Serum Cr reverted to baseline within 3 days of stopping the CEE.

### DISCUSSION

Renal allograft dysfunction is a common complication post-transplantation and can lead to graft loss. Cr, a product of muscle breakdown, is widely used as a marker of renal function as it is excreted in the glomerulus and to a lesser extent the proximal tubule. Cr level is dependent on muscle mass but can be increased by drugs such as trimethoprim and cimetidine through inhibition of tubular secretion or reduced in liver failure.

Creatine is an ingredient found in fish and meat and is readily available as supplements in CM and CEE forms, with CM being most widely used [1]. CM is well-studied with trials suggesting safety when taken at doses of 5–20 g/day [2]. As it is not degraded during digestion, and 99% is taken up by muscle or excreted into urine, serum Cr is unaffected [1]. Its side effects include minor gastrointestinal upset and one reported case of interstitial nephritis where it was taken at a large dose of 20 g/day for 4 weeks [3].

CEE, also known as creatine ester, is a form of CM with an ester attached in order to increase its bioavailability. CEE has a comparable creatine content to CM [1], and due to reduced acid stability is rapidly broken down and absorbed as Cr in the gastrointestinal tract, resulting in increased serum Cr [4], rendering serum Cr no longer a viable surrogate for glomerular filtration rate (GFR).

Our experience with this patient is consistent with the known pharmacokinetic differences between CM and CEE: there was no discernible change from baseline in measured serum Cr during the 6 months of 5 g/day CM, followed by an acute rise in Cr following the switch to 3.2 g/day CEE. Both supplements were taken within recommended dose ranges.

We report this case to raise awareness of a commonly ingested, performance-enhancing supplement, CEE, which may

give rise to an elevated serum Cr resembling that of advanced renal dysfunction. Where there is clinical uncertainty, an alternative assessment of GFR using cystatin C, iothalamate, iohexol or 51Cr-EDTA can be considered [5]. We also re-emphasize the importance of taking a detailed drug history.

### ACKNOWLEDGEMENTS

We thank the patient for allowing the publication of his clinical details. Patient consent has been obtained for the use of the clinical details in this case report.

### CONFLICT OF INTEREST STATEMENT

None declared.

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